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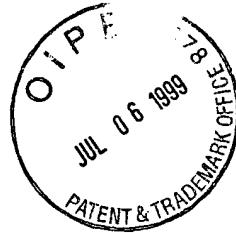
Applicant: **Malmros, et al.**

Application Number: **09/306,662**

Filing Date: **05/05/99**

Group Art Unit: **1651**

Title: **Method of in situ diagnosis by spectroscopic analysis  
of biological stain compositions**



**Information Disclosure Statement**

Hon. Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

The undersigned herewith submits in the above identified patent application a *revised* Information Disclosure Statement to comply with 37 CFR 1.98 (MPEP 609) and includes copies or abstracts (Medline) of all literature cited in the IDS submitted with the application. Those U.S. Patents for which the applicants feel are most relevant to the subject matter have been enclosed in the form of the "full-text database" format (rather than the "image" format).

Respectfully submitted,  
For the applicants,

A handwritten signature in black ink, appearing to be "M K Malmros", followed by a horizontal line.

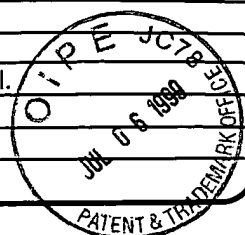
Mark K Malmros

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Substitute for form 1449B/PTO		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	09/306,662
		Filing Date	05/05/99
		First Named Inventor	Malmros, et al.
		Group Art Unit	1651
		Examiner Name	
		Attorney Docket Number	pro se
Sheet	1	of	4




OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
		AZARIAH J, et al. Studies on metachromasia. III. Toluidine blue-substrate interaction and metachromasia. Acta Histochem 1975;53(2):182-91	
		CANETE M, et al. Uptake and photoeffectiveness of two thiazines in HeLa cells. Anticancer Drug Des 1993 Dec;8(6):471-7	
		CANTO MI, et al. Methylene blue selectively stains intestinal metaplasia in Barrett's esophagus. Gastrointest Endosc 1996 Jul;44(1):1-7	
		CHESSER RS, et al. Primary cutaneous adenoid cystic carcinoma treated with Mohs micrographic surgery toluidine blue technique J Dermatol Surg Oncol 1992 Mar;18(3):175-6	
		DARZYNKIEWICZ Z, et al. Photosensitizing effects of the tricyclic heteroaromatic cationic dyes pyronin Y and toluidine blue O (tolonium chloride). Cancer Res 1988 Mar 1;48(5):1295-9	
		FOWLER GJ, et al. The photokilling of bladder carcinoma cells in vitro by phenothiazine dyes. Photochem Photobiol 1990 Sep;52(3):489-94	
		FUKUI I, ET AL In vivo staining test with methylene blue for bladder cancer.. J Urol 1983 Aug;130(2):252-5	
		HERLIN P, et al. A study of the mechanism of the toluidine blue dye test. Endoscopy 1983 Jan;15(1):4-7	
		HUGLIN D, et al. [Spectroscopic and thermodynamic investigations on the binding of azure B to chondroitin sulfate and the structure of the metachromatic dye complex]. Histochemistry 1986;86(1):71-82	
		JOURA EA, et al. Differentiating vulvar intraepithelial neoplasia from nonneoplastic epithelial disorders. The toluidine blue test. J Reprod Med 1998 Aug;43(8):671-4	
		KIRALY K, et al. Application of selected cationic dyes for the semiquantitative estimation of glycosaminoglycans in histological sections of articular cartilage by microspectrophotometry. Histochem J 1996 Aug;28(8):577-90	

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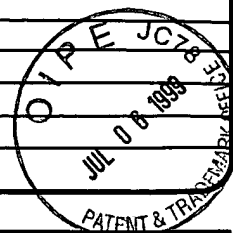
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		KLEEMANN D Experimental studies for photodynamic therapy of malignant tumors of the mouth cavity, larynx and pharynx with the photosensitizer methylene blue Laryngorhinootologie 1990 Aug;69(8):437-9	
		KONIG K, et al. Photochemotherapy of animal tumors with the photosensitizer methylene blue using a krypton laser. J Cancer Res Clin Oncol 1987;113(3):301-3	
		LAMPIDIS TJ, et al. Selective killing of carcinoma cells "in vitro" by lipophilic-cationic compounds: a cellular basis. Biomed Pharmacother 1985;39(5):220-6	
		LUNN G, et al. Removal of biological stains from aqueous solution using a flow-through decontamination procedure. Biotech Histochem 1994 Jan;69(1):45-54	
		MARSHALL PN The composition of stains produced by the oxidation of Methylene Blue. Histochem J 1976 Jul;8(4):431-42	
		MARTIN IC, et al. The application of toluidine blue as a diagnostic adjunct in the detection of epithelial dysplasia. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998 Apr;85(4):444-6	
		MARTIN, et al. Oxygen radicals are generated by dye-mediated intracellular photooxidations: a role for superoxide in photodynamic effects. Arch Biochem Biophys 1987 Jul;256(1):39-49	
		MELLO ML Optical anisotropy of toluidine blue-stained transformed cell nuclei. Acta Histochem 1995 Apr;97(2):159-64	
		MOHR H, et al. Virus inactivation of blood products by phenothiazine dyes and light. Photochem Photobiol 1997 Mar;65(3):441-5	
		ORTH K, et al. Photodynamic therapy of small adenocarcinomas with methylene blue]. Chirurg 1995 Dec;66(12):1254-7	
		O'TOOLE DK The toluidine blue-membrane filter method: absorption spectra of toluidine blue stained bacterial cells and the relationship between absorbance and dry mass of bacteria. Stain Technol 1983 Nov;58(6):357-64	

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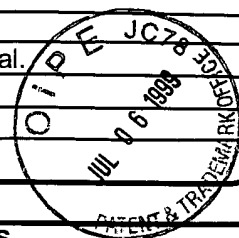
# **INFORMATION DISCLOSURE STATEMENT BY APPLICANT**

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Sheet 3 of 4

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		PAARDEKOOPER, et al. Intracellular damage in yeast cells caused by photodynamic treatment with toluidine blue. Photochem Photobiol 1995 Jan;61(1):84-9	
		PORTER, et al. Topical vital staining of human squamous cell carcinoma xenografts in nude mice. Laryngoscope 1988 Jul;98(7):734-9	
		ROTHMANN C, et al. Spectral imaging for quantitative histology and cytogenetics. Histol Histopathol 1998 Jul;13(3):921-6	
		RUIZ MORENO JA, et al. [The results of a selective program to detect intraepithelial neoplasms of the vulva]. Ginecol Obstet Mex 1992 Feb;60:55-9	
		SAMUEL I The action of dyes on tumors. Virologie 1978 Jul-Sep;29(3):213-8	
		SCHEUNER G, et al. [Metachromasia, double refraction and dichroism caused by Toluidine Blue reaction]. Prog Histochem Cytochem 1975;7(2):1-73	
		STOCKERT JC, et al. X-ray microanalysis of toluidine blue stained chromosomes: a quantitative study of the metachromatic reaction of chromatin. Histochemistry 1991;95(3):289-95	
		STOCKERT, et al. Photodynamic damage to HeLa cell microtubules induced by thiazine dyes. Cancer Chemother Pharmacol 1996;39(1-2):167-9	
		SUGERMAN HJ, et al. Diagnostic staining of neoplastic skin lesions with toluidine blue. Arch Surg 1970 Mar;100(3):240-3	
		TEMPLETON DM The basis and applicability of the dimethylmethylene blue binding assay for sulfated glycosaminoglycans. Connect Tissue Res 1988;17(1):23-32	
		THETHI K, et al. Determination of cell surface charge by photometric titration. J Biochem Biophys Methods 1997 Mar 27;34(2):137-45	

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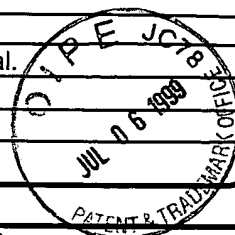
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Sheet 4 of 4

### Complete if Known

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		TROILIUS A, et al. Reflectance spectrophotometry in the objective assessment of dye laser-treated port-wine stains. Br J Dermatol 1995 Feb;132(2):245-50	
		WAINWRIGHT, et al. A study of photobactericidal activity in the phenothiazinium series. FEMS Immunol Med Microbiol 1997 Sep;19(1):75-80	
		WAINWRIGHT, et al. Photobactericidal activity of phenothiazinium dyes against methicillin-resistant strains of Staphylococcus aureus. FEMS Microbiol Lett 1998 Mar 15;160(2):177-81	
		WARNAKULASURIYA, et al. Sensitivity and specificity of OraScan (R) toluidine blue mouthrinse in the detection of oral cancer and precancer. J Oral Pathol Med 1996 Mar;25(3):97-103	
		WEISHAUP, et al. Identification of singlet oxygen as the cytotoxic agent in photoinactivation of a murine tumor. Cancer Res 1976 Jul;36(7 PT 1):2326-9	
		WILSON, et al. Sensitisation of Candida albicans to killing by low-power laser light. J Oral Pathol Med 1993 Sep;22(8):354-7	
		YANG R, et al. [Methylene blue staining in fiberoptic bronchoscopy in the diagnosis of bronchial tumors]. Chung Hua Wai Ko Tsa Chih 1996 Mar;34(3):167-9	
		ZHOU R, et al. A multiple wavelength algorithm in color image analysis and its applications in stain decomposition in microscopy images. Med Phys 1996 Dec;23(12):1977-86	

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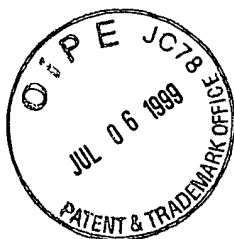
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